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DEMONSTRATION OF MICROCOCCI IN THE BONES IN RICKETS AND SCURVY

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Additions to our knowledge of the factors concerned in the production of scurvy are being made as the subject is studied from various standpoints. That an unsuitable diet lays the foundation for the development of scurvy is generally accepted. Just what constitutes this unsuitability is one of the questions for which an answer has long been sought. As to the condition produced in guinea-pigs on certain diets, McCollum says that "only those diets which produce feces of a character readily eliminated will relieve or prevent the disease." He was able to prevent the development of scurvy in guinea-pigs fed on oats and milk by giving with it a liberal amount of liquid petroleum, and also to effect a complete cure in animals in advanced stages without change of diet by the use of petroleum. McCollum therefore concludes that scurvy in the guinea-pig is the result of the retention of feces, but whether this is the case in human scurvy or not is unknown. As to the explanation of the structural changes present he is unable to make any statement.

Hess,[1] from a study of necropsy records of cases of scurvy and from clinical records of his own cases, concludes that in human scurvy constipation plays a secondary rôle. He believes that a faulty diet permits intestinal bacteria to elaborate toxic substances which may not always be alike; he remarks the striking susceptibility to infections and thinks some of the hemorrhages are secondary while others are of scorbutic origin.

The difficulty in the way of arriving at the etiology of scurvy and allied conditions may perhaps be due to their dependence on more than one factor. It seems quite possible that the unsuitable diet may bring about a condition in the body which renders it susceptible to infectious agents of low virulence, which under other conditions would not occur. To study the problem from this view-point seems warranted.

Important as the diet must be in any investigation of the etiology of scurvy, bacteriologic and microscopic studies should not be neg-

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[1] Am. Jour. Dis. Child., 1917, 14, p. 337.

lected. A very careful study[2] of the lesions produced in experimental scurvy lead to the belief that bacteria in some way were related to the lesions. That they are the cause of the changes needs further demonstration, but that they are present is evidenced both by the results of cultures[3] and the microscopic examination of the tissues.

I have had the opportunity to study the changes in bones, presenting signs of rickets or scurvy, from different sources. The material includes bones from 3 human cases, tissues from 5 puppies with mild evidences of scurvy, and from 1 guinea-pig with rather advanced lesions, apparently developed spontaneously under ordinary conditions. A comparison of the changes found in the different cases may be of interest.

The human specimens were obtained through the kindness of Dr. E. R. LeCount and Dr. A. M. Moody. In two of the cases there were well defined rachitic changes in the bones.

CASE 1.—A colored child, 13 months old, was admitted to St. Luke's Hospital, Feb. 2, 1916, to the service of Dr. Brenneman. A diagnosis of gastro-enteritis and rickets was made. The child died Feb. 11.

Extracts from the Postmortem Record: The anterior fontanelle is 3 cm. long by 2.7 cm. wide. The two lower central incisors are partially erupted. There are no other teeth. There is a marked rachitic rosary and marked enlargement and deformity of the heads of the long bones. The abdomen is distended. The mesenteric lymph nodes are distinctly enlarged. The epiphyseal lines of the long bones as well as the ribs are irregular and very much broadened. They contain an increased amount of cartilage. On microscopic examination the margins of the costal cartilage are very irregular and the zone of ossification broad. The diameter of the rib in this region is about twice the normal. A rather large amount of osteoid tissue is present particularly at the periphery where it apparently replaces portions of the compact bone. Near the costochondral junction and for a considerable distance from it, the marrow cells are much diminished in numbers, small hemorrhages are numerous, as are also small amounts of fibrin. In sections stained by Gram's method and also by methylene blue, cocci are found in small areas of degeneration, located here and there along the margin of the bone and cartilage and seemingly always involving a blood vessel. The organisms are found both within the vessels and in the surrounding tissues. Farther from the cartilage the marrow is more normal in appearance. It is very hyperemic and many eosinophil cells are scattered through it.

CASE 2.—Child, 1 year old, admitted to Cook County Hospital, April 24, 1916, to the care of Dr. Michael. According to the clinical record the child was breastfed the first 3 months; after that Borden's milk was given. The child had always been fretful and the last 2 weeks had coughed a good deal. There were râles posteriorly on both sides, temperature 105 F., respiration rapid, and patches of bronchial breathing. The child died 5 days after entrance.

Anatomic Diagnosis: Rachitic osteochondritis; "pigeon breast," hyperplasia of the spleen, cervical, tracheobronchial, periaortic and mesenteric lymph glands;

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[2] Jackson, L., and Moore, J. J.: Jour. Infect. Dis., 1916, 19, p. 478.

[3] Jackson, L., and Moody, A. M.: Ibid., p. 511.

marked general anemia; slight cloudy swelling of the kidneys; marked fatty changes in the liver; atelectasis and compensatory emphysema of the lungs; localized, left, fibrous pleuritis.

Sections of the ribs from this case prepared for microscopic examination include the costochondral junctions which are greatly increased in diameter. Large, irregularly rounded masses of cartilage extend for some distance into the marrow cavity, and for even greater distances at the periphery of the bone. The compact bone in these places has a fragmented appearance and is partially replaced by osteoid tissue. The bone marrow for a distance of 1.5 cm. from the cartilage is almost completely replaced by fibrous tissue and even where more normal marrow is found it occurs in larger or smaller patches surrounded by fibrous tissue. Scattered through the bone marrow spaces are many small hemorrhages. In some of these and also in the surrounding tissue and in occasional thrombosed vessels, cocci are found and sometimes they were quite numerous. In sections stained with phosphotungstic acid hematoxylin, small amounts of fibrin are found in these locations.

CASE 3.—The material was obtained from a colored infant, dying 3 hours after birth. The Wassermann reaction of the mother was negative and no spirochetes were found in Levaditi preparations of the tissues of the infant. The only gross changes were enlargement of the costochondral junctions and the ends of the long bones. The ribs were increased in width at the costochondral junctions and the epiphyseal junctions were somewhat widened. In sections of the rib the cartilaginous margin is very irregular. Prolongations of cartilage extend down into the marrow cavity and at the periphery these form large rounded masses. There is a marked decrease in the normal marrow cells in the region bordering on the cartilage and for about a centimeter from it, and a rather marked increase in the amount of fat. There are a number of small hemorrhages present. In the upper portion of the tibia the changes are not so marked. The epiphyseal line is fairly distinct but somewhat irregular. There are, however, hemorrhages into the bone marrow and in places a rather marked degenerative process in the cells and some of the bony trabeculae. Cocci were occasionally found along the margins of bone and within and about blood vessels.

The prominent features in these cases are: increased width at the costochondral and epiphyseal junctions; a broad zone of ossification; replacement of bone marrow cells by fibrous tissue and of bone by osteoid tissue; many hemorrhages, and small typical regions of degeneration in which small cocci often were found.

The 5 puppies examined were from two litters, 1 from the first and 4 from the second. The puppies of the first litter, when purchased, were thin but otherwise appeared normal. Although well fed and cared for, they gradually became thinner and finally died. At postmortem examination of the last one of these animals, well marked enlargements of the costochondral junctions of the ribs were discovered. Doubtless intestinal worms were present in this case but were not found on account of failure to examine the intestines. This dog at the time of death was about 4 months old and had received no treatment. The members of the second litter appeared healthy and well nourished when purchased, but they also gradually lost flesh; two of them died and two were killed. In all of these the intestinal tract and stomach contained numerous worms (Ascaris camis), and in all of the puppies there were mild changes in the bones. Otherwise there were no noteworthy gross changes. The age of these animals was about 2 months and they had received no treatment.

The bone changes in all of these animals were mild and necessarily of short duration. The alterations found in the one mentioned first were slightly more advanced but typical of all and will therefore be described in some detail. There is rather abrupt swelling at the costochondral junction to about twice the normal diameter. The margin of the cartilage is slightly irregular and there is a definite line of demarcation between the cartilage and bone. There is slight rarefaction of the marrow in this region, more marked at the periphery, together with small hemorrhages and edema. There are numerous small lesions in the bone marrow in which are degenerative changes in the endothelial and marrow cells, fibrin formation and often hemorrhage. These lesions are in close relationship to blood vessels and bone especially along the edge of the compacta and between the periosteum and the bone. In this type of lesion cocci are quite frequently found. It should be mentioned here that the regional lymph glands in these dogs are hemorrhagic and microscopically present an appearance quite similar to those found in experimental scurvy in guinea-pigs.

It will be noted that the changes in the puppies are apparently milder and of shorter duration than in the human cases, but that in other respects there is a rather close resemblance.

The guinea-pig examined was one that seemingly had contracted the disease spontaneously. Three weeks before it was killed the pig had been injected with urine from a case of nephritis. No swelling of the joints was noticed at the time of injection, but judging from the appearance of the lesions the beginning of the process in the joint must have preceded the injection by a considerable length of time. At necropsy it was noticed that one of the wrist joints was decidedly enlarged and that the costochondral junctions were swollen. There were hemorrhages about the joint and the corresponding axillary lymph glands were enlarged and hemorrhagic. So far as known this pig had always received the ordinary diet for guinea-pigs. Examination of microscopic preparations of the wrist joint revealed the presence of extensive alterations in the ends of both the ulna and radius. The marrow was almost entirely replaced by a well developed fibrous tissue and at the periphery of the bones in the region of the epiphysis there were still large areas of necrosis. There was a decrease in the amount of change present as the proximal ends of the bones were approached. Even in these bones where the changes appeared oldest there were the typical small lesions indicating that the process was still active. In the small bones of the wrist the process appeared more recent. There was little fibrous tissue replacing the marrow but there was much hemorrhage and edema. The changes in the rib examined were mild. It is apparent that the changes just described are identical with those found in moderately severe cases of experimental scurvy.

SUMMARY

In the cases considered in this paper there appear rather marked differences in the acuteness and severity of the process. The appearance in the human cases is that of a subacute process continued over a rather long period of time. There are no large amounts of necrosis such as are seen in the guinea-pig, although this feature may have

been more prominent at some stage in the disease. In fact, they present much the same appearance as some of the older healing cases of experimental scurvy in guinea-pigs. The changes in the bones of the puppies are the mildest and suggest a subacute process operating for a shorter length of time and in this respect resemble more closely the changes found in the infant.

The location of the alterations is the same in all the cases, the most noticeable feature being the increase in diameter at the junction of cartilage and bone with most pronounced changes at the periphery, and the relation of changes to blood vessels and bone.

The changes invariably present are hemorrhage, edema, and more or less degeneration of the endothelial and marrow cells and bone.

The similarity in the nature of the process producing the alterations in all of these cases is quite striking. Wherever it is active there is more or less degeneration of cells with fibrin formation, usually involving a blood vessel and often accompanied by hemorrhage. It is in these places that micrococci are often seen. A distinctive feature of all of these cases is the absence of any marked cellular exudate in relation to the lesions at any stage of the disease. There is first degenerative changes in the cells and bone followed by disappearance of normal cells and replacement by fibrous tissue.

While we cannot as yet state positively that the lesions described are due directly to the action of the micrococci so frequently found in connection with the lesions, and particularly the fresh ones, the presence of cocci appears at least significant. Even should we subsequently decide that these organisms are but secondary invaders it still seems that the evidence presented by microscopic preparations of the lesions argues for the presence of some infectious agent, and emphasizes the need of further work on the bacteriology of these conditions.